Remarks

Status and Disposition of Claims

This Amendment is responsive to the Office Action mailed May 4, 2010. In the Action, the Office considered claims 1-6, 10-13, 15, and 16, with claims 7-9 and 14 having been withdrawn from consideration as directed to a non-elected invention.

With this Amendment, Applicants amend claim 1 and add new claims 21-23. Thus, with this amendment, claims 1-6, 10-13, and 15-23 remain pending and under consideration. Applicants allow claims 7-9 and 14 to remain pending, as they are subject to possible rejoinder.

The amendment to claim 1 finds support in paragraphs [0019], [0021], and [0022], as shown below (emphasis added), and does not add new matter.

> [0019]
>
> The present invention will be described in detail below.
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> The composite porous membrane of the present invention comprises at least one porous membrane containing an organic polymer and at least one supporting porous membrane adjacent thereto.
>
> *The composite porous membrane may have a structure wherein a porous membrane is adjacent to and also adheres to a supporting porous membrane (a structure wherein a porous membrane penetrates into a supporting porous membrane).* Examples of such a structure may include: a bilaminar structure formed by integrating a single porous membrane with a single supporting porous membrane (that is, a structure consisting of "porous membrane/supporting porous membrane"); a trilaminar sandwich structure wherein porous membranes are located on both sides of a supporting porous membrane (that is, a structure consisting of "porous membrane/supporting porous membrane/porous membrane"); a trilaminar sandwich structure wherein supporting porous membranes are located on both sides of a porous membrane (that is, a structure consisting of "supporting porous membrane/porous membrane/supporting porous membrane"); and a trilaminar structure wherein two porous membrane layers are present on either one side of a supporting porous membrane (that is, a structure consisting of "porous membrane/porous membrane/supporting porous membrane"). A bilaminar structure formed by integrating a single porous membrane with a single supporting porous membrane (that is, a structure

consisting of "porous membrane/supporting porous membrane") is preferable because it is easily produced.

[0021]

The composite porous membrane of the present invention is characterized in that an organic polymer constituting the porous membrane penetrates into a supporting porous membrane at least in a part of the supporting porous membrane flat surface adjacent to the porous membrane. For example, when the supporting porous membrane constituting the composite porous membrane is a non-woven fabric, *if the surface of the porous membrane in the composite porous membrane is observed under an electron microscope, a state (clogging pore structure) where the shape of a pore is distorted or such a pore is occluded on the back side of the porous membrane (supporting porous membrane side) can be seen as a result of the porous membrane penetrating into a part of the non-woven fabric plane (a fibrous portion or an entangled fiber portion).*

That is to say, in the composite porous membrane of the present invention, since the organic polymer constituting the porous membrane penetrates into a part of the supporting porous membrane, such a part of the supporting porous membrane (which is, for example, fibers constituting a non-woven fabric) decreases the through-pore percentage of the porous membrane and occludes pores (such a state is shown in Figs. 1 and 2). As a result, it is extremely rare that all the pores of the porous membrane are through-pores.

In the composite porous membrane of the present invention, the percentage of through-pores in the porous membrane is 30% or more, preferably 40% or more, more preferably 50% or more, and most preferably 60% or more. If the ratio of such through-pores is less than 30%, not only a filtration rate or the contact efficiency between different cells separated from each other decreases, but also targets generally passing through such through-pores remain incorporated into clogging pores and captured therein. Thereby, the size separation effect decreases. It is to be noted that the percentage of through-pores in the porous membrane is also affected by membrane formation conditions (for example, the concentration of a hydrophobic organic solvent solution to be casted, the amount casted, the type of a solvent, etc.).

[0022]

In the present invention, the term "through-pores" of the porous membrane is used to mean that when any given pore P is focused in the porous membrane, if the area of the pore P that is actually measured in the electron photomicrograph of the porous membrane flat surface (for example, when the shape of a pore is round, the value of $(D/2)^2\pi$ calculated from the diameter D of the pore) is defined as S(P), *the area of a region (so-called through region)*

wherein the structure of the supporting porous membrane located on the other side can be observed through the pore P makes up 70% or more of S(P).

Applicants submit that claims 21-23 find support in original claims 1-3 and in paragraphs [0020], [0022], and [0024].

Information Disclosure Statements

Applicants again respectfully note that a Supplemental Information Disclosure statement was filed July 14, 2006, but that the Examiner's consideration of this Statement does not appear to be reflected in the record. *Applicants respectfully request that the Examiner indicate such consideration in the next official communication.*

Restriction Requirement

The Office withdraws claims 7-9 and 14, as drawn to a non-elected invention. Applicants allow claims 7-9 and 14 to remain pending, as they are subject to possible rejoinder.

Claim Rejections – 35 U.S.C. § 103

The Office Action rejects claims 1-6 and 17-20 under 35 U.S.C. § 103 as allegedly obvious over JP 2003-149096, to Tanaka et al. in view of U.S. Application Publication No. 2003/0150808, to Morikawa et al., as evidenced by U.S. Application Publication No. 2006/0097361, to Tanaka et al. (hereinafter '361) and U.S. Patent No. 4,992,485, to Koo et al. The Action further rejects claims 10-13 over Tanaka et al., Morikawa et al., and U.S. Patent No. 6,645,388, to Sheikh-Ali et al. The Action further rejects claims 15 and 16 over U.S. Patent No. 5,665,596, to Mussi et al., in view of Tanaka et al. in view of Morikawa et al., as evidence by JP 2001-157574, to Shimomura et al.

Applicants respectfully disagree with the rejections for the reasons previously presented as well as those that follow.

Initially, Applicants respectfully note that the non-final Office Action had clearly misinterpreted the claims, a point that was raised in Applicants' prior response. Applicants had expressly requested that if the art-based rejection was maintained, that the Office clearly explain

where each of the features of Applicants' claimed invention could be found in the cited art. *Applicants again expressly request that the Office explain where the claimed features can be found, or how they are rendered obvious by, the cited art.*

The Present Invention

Applicants will begin addressing the rejection by reviewing again features of the present invention.

The porous membrane of the present invention has a characteristic structure in which a part of the supporting porous membrane penetrates into the honeycombed structure membrane. (The rejection finds the honeycombed structure of Tanaka et al. to satisfy this element). When the supporting porous membrane is a nonwoven fabric, for example, a part of the fibers that constitute the nonwoven fabric adheres to or penetrates into the honeycombed structure membrane, which unifies the honeycombed membrane with the fibers. This structure exhibits noticeably advantageous effects by tightly combining a porous membrane with a supporting porous membrane that are not easily separated from each other. In addition, the structure of the porous membrane of the present invention is particularly suitable for effective co-culture of cells because the cells introduced into the supporting porous membrane, e.g., a nonwoven fabric, can easily arrive at or make contact with the honeycombed structure membrane by moving along the nonwoven fabric (cell movement may occur due to the injection of the cells as water-flow or the movement accompanied by the proliferation of cells during cultivation).

Another feature of the present invention is that the way in which contact between the porous membrane and the supporting porous membrane can be observed by microscopic observation from the surface of the porous membrane (amended claim 1; see Figure 1 of the specification and highlighted sentence of [0021] shown above). The observation confirms that the porous membrane firmly adheres to the surface of the supporting porous membrane (or the surface of a fiber in case of non-woven fabric) in a manner similar to fusion binding.

On the other hand, Morikawa et al. teaches that "[t]he resin permeating into the porous substrate is firmly fixed on the porous substrate by the so-called 'anchor effect'" in paragraph [0029]. As one can see from the Figures presented Morikawa et al., however, such adhesion

cannot be confirmed by micrographic images taken from the surface of the porous resin layer, but can be confirmed only by a cross-sectional image of the composite porous membrane. Accordingly, the structure of the composite porous membrane of the present invention is different from that of Morikawa et al.

The difference between the composite porous membrane of the present invention and that of Morikawa et al. is explicitly described in paragraph [0020] of the specification of the present specification. In particular, the highlighted sentence below exactly corresponds to the composite porous membrane of Morikawa et al. (a porous body having continuous pores in a three-dimensional network state that is mainly obtained by the phase separation method).

> [0020] . . .
>
> Membranes, whose opening ratio, D, σd, the percentage of through-pores, T, and internal membrane structure can not be experimentally determined, are excluded from the porous membrane of the present invention. For example, in the case of a non-woven fabric that is preferably used as a supporting porous membrane or *a porous body having continuous pores in a three-dimensional network state that is mainly obtained by the phase separation method*, it is difficult to determine the aforementioned factors by the methods described in examples. Accordingly, these products clearly differ from the porous membrane of the present invention.

Morikawa et al. discloses, in its Examples, that they measured average sizes of micropores by the images from scanning electron microscopy. As seen from microscopic images of Figure 1 and 3, however, the structure of the membrane surface is irregular, and it is hard to understand how they measured or calculated the average sizes of micropores, but it is not disclosed in the specification of Morikawa et al.

<u>Persons Skilled in the Art Would Not Combine the Disparate Teachings of Tanaka et al. and Morikawa et al.</u>

Applicants further respectfully note that the composite membrane of Morikawa et al., which is targeted wastewater purification, is required to have a high performance at a pressure as high as possible so that a large amount of wastewater can be efficiently processed. Consequently, the composite membrane of Morikawa et al. is purposefully designed with a pore

resin layer with about 100 micron thickness so as to tolerate the high pressure in the use of the water treatment.

On the other hand, the goal of the present invention, as well as Tanaka et al. is cell separation (blood filtration or a diaphragm for cell co-culture), and it is targeted to the medical field. For medical applications, damage to cells must be minimized for efficient culture of cells, and thus the pressure exerted upon the membrane substrate must be as low as possible. The honeycombed structure membrane is the best choice for this purpose because it is superior in its (high) surface opening ratio, high vacancy ratio, and thickness (about 5 micron). However, the physical strength of the honeycombed structure membrane was very low, and thus the improvement in the membrane strength had been a critical problem to a person skilled in the art to which the invention pertains.

Applicants respectfully submit that because the strength of the membranes and the pressures applied to the membrane are significantly different between the uses in the medical fields and the water treatment fields, a person skilled in the art would not have thought to combine the teachings of Morikawa et al. with those of Tanaka et al. in order to solve the problem of reinforcement to honeycombed structure membranes. Additionally, a person skilled in the art would understand that the problem of the honeycombed structure membrane cannot be solved by simply combining it with the teaching of Morikawa et al., which uses a porous resin layer for the application to water treatment, because the strength of membranes and the pressure applied to the membranes are very different.

<u>Combining Morikawa et al. With Tanaka et al. Would Not Yield the Present Invention</u>

Applicants note that the following points were raised in the prior response, and have yet to be addressed by the Office. *Applicants raise the points again and specifically request that the Office address them in the next communication.*

Applicants respectfully submit that even Tanaka et al. and Morikawa et al. were combined, the present invention would not result. The production method of Morikawa et al. requires at least two steps: (1) applying stock solution of the porous resin layer onto one side or both sides of a porous substrate (polyester nonwoven fabric in Example 1) and then (2)

immersing it into a non-solvent, as disclosed in Example 1. However, it is practically impossible to perform such a process unless the viscosity of the stock solution is sufficiently high because it is very difficult to retain the stock solution on or in the porous substrate until the process proceeds to step (2). The viscosity of the stock solution disclosed in Example l of Morikawa et al. (the solids content concentration of 18.5 weight%) cannot be accurately determined because the molecular weight of PVDF is not disclosed; however, it is clear from the description in Comparative Example 2 that it has a low fluidity and a high viscosity, such that the applied stock solution can hardly be immersed into the inside of nonwoven fabric. Comparative Example 2 of Morikawa et al. discloses that when the stock solution was applied onto a nonwoven fabric with a density of 0.90 g/cm^3, no composite layer was observed on the finally obtained separation membrane, but only a porous resin layer was placed on the substrate, and the porous resin layer was found to be detached from the porous substrate after a permeation test. These disclosures suggest that the stock solution has a low fluidity and a high viscosity and the stock solution applied on nonwoven fabric can hardly be immersed into the inside of the nonwoven fabric. That is, the method of Morikawa et al. can only be carried out when the viscosity of the stock solution is high enough to be applied onto the surface of a porous substrate (nonwoven fabric) (or high enough to be adequately immersed into the porous substrate).

On the other hand, the method of Tanaka et al. uses, as disclosed in Example 1, a diluted stock solution with a polymer concentration of 0.1 to 2 weight% (chloroform as solvent). The stock solution with such a diluted concentration has a fluidity identical to water, so the movement or loss of the stock solution must be prevented until it forms a membrane structure by casting it on the liquid-repellent substrate, such as glass (glass plate), agarose gel, or mica. However, such a stock solution with a high fluidity cannot he casted on the surface of a porous substrate such as nonwoven fabric because the stock solution would permeate into or flow out of the nonwoven fabric. Comparative Example 3 of the present application corresponds to the situation in which the stock solution was casted on nonwoven fabric so as not to flow out the stock solution. Electron micrograph observation for the product after the removal of chloroform revealed that a proper composite porous membrane was not formed by using this procedure. The blockage of the pores occurred because chloroform dried up with the stock solution retained inside of the nonwoven fabric, and the break of porous membrane was frequently observed near

the surface of the nonwoven fabric due to many undulations in the surface of the nonwoven fabric.

Unexpected/Meritorious Effects/Advantages Obtained by the Present Invention

As recited by amended claim 1, the present invention includes a composite membrane having a structure in which the supporting porous membrane located on the other side can be observed through pores of the porous membrane by a microscope observation from the surface of the porous membrane. This feature, in combination with the other recited features, produces noticeably outstanding advantageous effects, particularly in cell co-culture.

The composite membrane of the present invention enables one to observe living cells from the surface of the pore membrane during cell co-culture, thereby confirming the proliferation and condition (around the pore membrane) of the first cells introduced into the support porous membrane (or non-woven fabric). Another advantage to a person skilled in the art to which the invention pertains is that the composite membrane of the present invention allows determination of an appropriate time for introducing second cells onto the pore membrane, while he or she observes the condition of first cells beforehand. A further extremely important advantageous effect is that the composite membrane of the present invention enables one to simultaneously observe first and second cells after the introduction of the second cells, which is extremely important for a microscopic observation, particularly when it is processed in a form of "cup-type culture apparatus" as disclosed in Examples of the specification.

Conclusion

In view of the foregoing, Applicants respectfully submit that a person skilled in the art would not have combined the disparate teachings of Tanaka et al. and Morikawa et al. as suggested by the Office, and even if the teachings were combined, the present invention would not result. Moreover, Applicants respectfully submit that the present invention produces unexpectedly good results, which could not have been expected based on the prior art.

Applicants respectfully request withdrawal of the obviousness rejections.

Conclusion

In view of the foregoing remarks and amendments, Applicants respectfully request withdrawal of the rejections of record and allowance of the claims. If the Examiner has any questions or wishes to discuss this application further, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

The Patent and Trademark Office is hereby authorized to charge Deposit Account No. 19-0089 any fee necessary to ensure consideration of this paper.

Respectfully Submitted,
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